

**DETAILED ACTION**

***Response to Arguments and Amendments***

1. The response filed 11/06/09 has been entered.
2. Applicant's arguments filed 11/06/09 have been fully considered but they are not deemed to be persuasive.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. Claims 1, 4-20, 23-32 and 38-40 are pending in this office action. Claims 1, 7-12 and 38 are currently amended.
5. The rejection of claims 1, 6-15 and 17-19 under 35 U.S.C. 102(b) as being anticipated by Hammes et al. (US 3,652,290) is withdrawn based on the amendment to the claims and also because Hammes fails to teach that their population undergoes radiation therapy.
6. The rejection of claims 1, 4-9, 10-19 and 26-32 under 35 U.S.C. 103(a) as being unpatentable over Campbell (US 6,187,817) in view of Gabrilove, (US 4,961,926) further in view of Kil et al., (WO 03/045334) is withdrawn based on the amendment to the claims and Applicant's argument that Campbell fails to teach treating oral mucositis

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in patients undergoing radiation therapy, and that Gabrilove's agent used has a molecular weight of 20,000. In summary none of the patents teach the use of reducing oral mucositis in patients undergoing radiation therapy.

7. The rejection of claims 38-40 under 35 U.S.C. 103(a) as being unpatentable over Campbell (US 6,187,817) in view of Gabrilove (US 4,961,926 ) and further in view of Kil et al. (WO 03/045334) as applied to claims 1, 4-9, 10-19 and 26-32 is withdrawn based on the amendment to the claims and Applicant's argument that Campbell fails to teach treating oral mucositis in patients undergoing radiation therapy and that Gabrilove's agent used has a molecular weight of 20,000. In summary none of the patents teach the use of reducing oral mucositis in patients undergoing radiation therapy.

### ***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 4-19 rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US Patent 6,265,386) as evidence by Pusztai et al. (US Patent 6,110,891).

Campbell teaches a method of reducing gastrointestinal toxicity, in patients undergoing cancer chemotherapy (i.e., a cancer patient) and undergoing radiation therapy by administering the protective agents D-methionine, L-methionine, a mixture of D and L methionine and a pharmaceutically acceptable salt thereof (see col. 1, lines 12-35, col. 15, lines 25-30 and col. 19, lines 6-8, as required by instant claims 1, 4-6 and 13). Campbell also teaches that the methionine protective agent may be administered orally, and should be given in an amount that will result in a blood serum level equivalent to that achieved parenterally in doses ranging from 1.0 mg-500 mg/kg body weight. See col. 17, lines 44-47, col. 17, lines 30-56 and col. 24, lines 59- 65 (claims 13-17, 29-30). With regards to instant claims 18-19, once the amounts (i.e., 1.0-500 mg/kg body weight ) is administered, intrinsically it will maintain a blood serum level of protective agent within the patient of at least 10% or 20-70% of the blood serum level by administration of the effective amount of the protective agent. Campbell also teaches the protective agent is administered from 6 hours before to 6 hours after exposure to chemotherapeutic agent, within 1 hour before and 1 hour after chemotherapeutic agent and one-half hour (30 mins) before and after chemotherapeutic agent (as required by instant claims 7 and 10-12, see col. 20, lines 8-24). Campbell also teaches that the protective agent may be administered simultaneously and or subsequently with radiation (see col. 19, lines 9-15).

As to the limitation of reducing oral mucositis, Campbell is silent to the specific teaching (i.e., oral mucositis), nonetheless Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders. As evidence by Pusztai et al. "Mucositis is a painful and debilitating condition in which rapidly growing epithelial cells are damaged and the external mucous layer is removed and/or not replaced sufficiently quickly. Mucositis may result in infection by microorganisms which are present, for example in the mouth or gut. The condition is seen as a major side effect in the treatment of cancer. The incidence and severity of mucositis may increase with increasing rounds of cancer therapy, and may ultimately effect patient treatment compliance and survival", (see col. 1, lines 55-54). Specifically Pusztai teaches that chemotherapeutic agents and radiotherapy are agents that damage the mucosal cells, therefore it would have been obvious that Campbell's teachings of treating gastrointestinal symptoms in cancer patients would also reduce oral mucositis in a human or animal cancer patient undergoing chemotherapy because it is well known in the art that cancer patients undergoing chemotherapy and radiation are susceptible to destruction of the mucosal cell in the gut (gastrointestinal) and the mouth as evidence by Pusztai.

9. Claims 1 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US Patent 6,265,386) as evidence by Pusztai et al. (US Patent 6,110,891).

Campbell is applied here as above as it relates to claim 1.

Campbell further teaches that the chemotherapeutic effective amount of anti-tumor platinum coordination compound is cisplatin and the protective agent is D-methionine as required by instant claims 38-40, (see abstract).

As to the limitation of reducing oral mucositis, Campbell is silent to the specific teaching (i.e., reducing oral mucositis), nonetheless Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders. As evidence by Pusztai et al. "Mucositis is a painful and debilitating condition in which rapidly growing epithelial cells are damaged and the external mucous layer is removed and/or not replaced sufficiently quickly. Mucositis may result in infection by microorganisms which are present, for example in the mouth or gut. The condition is seen as a major side effect in the treatment of cancer. The incidence and severity of mucositis may increase with increasing rounds of cancer therapy, and may ultimately effect patient treatment compliance and survival", (see col. 1, lines 55-54). Specifically Pusztai teaches that chemotherapeutic agents and radiotherapy are agents that damage the mucosal cells, therefore it would have been obvious that Campbell's method would include reducing oral mucositis in a human or animal cancer patient undergoing chemotherapy because it is well known in the art that cancer patients undergoing chemotherapy and radiation are susceptible to destruction of the mucosal cell in the gut (gastrointestinal) and the mouth, as evidence by Pusztai.

***Double Patenting***

10. The rejection of claims 20 and 23-32 under the ground of nonstatutory patenting over claims 1-29 of copending Application No. 10694448 (now a US Patent 7,557,142 and 6,187,817), are withdrawn because claims 20 and 23-32 are cancelled. However, because of the amendment to the claims a new rejection is made.

11. Claims 1, 4-19 and 38-40 stand rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-9, 11-13,15-25 and 27-33 of U.S. application No. 10/694,432 for the reasons made of record in Paper No. 20090709.

Applicant argues that “the '432 application contains claims directed to methods for treating alopecia in a patient experiencing exposure to radiation by administering D-methionine, L-methionine, or a mixture of D- and L-methionine. Since the mechanism for alopecia and oral mucositis arising from radiation therapy are significantly different, none of the claims of the '432 application provides a reason to try methionine for treatment of oral mucositis in a cancer patient undergoing radiation therapy”.

In response contrary to Applicant’s assertion that the claims are directed to treating alopecia in a patient experiencing exposure to radiation by administering D-methionine or mixtures thereof. The issue is that the same drug formulation is administered to patients exposed to radiation who are suffering from cancer (as in the instant claims 1, 4-19 and 38-40).

Thus Applicant's arguments have been fully considered but they are not persuasive for the reason's given above.

12. Claims 1, 4-19 and 38-40 stand rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-29 of (US Patent 7,557,142) and claims 1-36 of (US Patent 6,187,817).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application is directed to treating diseases (reducing oral mucositis in a patient population undergoing chemotherapy and radiation) and the claims of in the instant claims '142 are directed to reducing the incidence of ototoxicity in a patient population undergoing chemotherapy with a chemotherapeutic effective amount of an antitumor platinum coordination compound (which is the same as in the instant claims). The claims of the '817 are directed to reducing the ototoxicity in a patient population undergoing chemotherapy with a chemotherapeutic effective amount of an antitumor platinum coordination compound (which is the same as in the instant claims). Since there is no separate defining step other than solely administering methionine for the treatment of conditions related to the use of chemotherapeutic effective amounts of an antitumor platinum coordination compound, because the same population are being treated one of ordinary skill in the art would reasonably expect the different conditions to also be treated in a population experiencing the effects of the same antitumor platinum coordination compound.

Radiation is commonly accompanied/combined with treatment of cancers (See evidence by Mori in its entirety).

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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/S. V. G./  
Examiner, Art Unit 1618  
1/08/10

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